Summary & Conclusion

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This thesis consists mainly of three chapters:

1- **The first chapter; the introduction,** contains two parts, the first one represents short notes about the physical and chemical properties of the drugs under investigation besides their mode of action and uses. The second part includes a literature survey on the previous works carried out for the determination of the drugs; sulfamethoxazole (Sul), lincomycin hydrochloride (Lin) and mebeverine hydrochloride (Meb), including spectrophotometric, spectroflourimetric, titrimetric, physicochemical, electrochemical and chromatographic methods of analysis.

2- **The second chapter; the experimental part,** describes the procedures used throughout the study so as to get the optimum conditions favouring coloured complex formation between the drug molecules as electron donors and various electron acceptor molecules (o-chloranil "I", chloranilic acid "II", 2,4 dinitrophenol "III", picric acid "IV" and 3,4 dinitrobenzoic acid "V"). This chapter also describes all instrument used in the work and how to prepare and elucidate the molecular structure of the solid CT complexes.

3- **The third chapter; results and discussion,** includes the representation of results obtained throughout the work and the explanation of them. It is subdivided to two major divisions:

3.A. Studies of complex in solution:-

In this part the optimum conditions that favour the formation of complexes were extensively studied. These conditions were then chosen for the microdetermination of the drugs under investigation.

(i) ***Britton*** and ***Rhobinson*** universal buffer solution was found to be the best media for complexation process. This series of buffer solutions has the advantage of wide range of pH (2 ~ 12) and its components do not seem to interfere with the drugs or reagents used.

It was found that, the maximum tendency of complex formation takes place at pHs 8.23, 5.25 and 11.15 for Sul with reagents I, III and IV, respectively. For Lin, the optimum pHs are 3.35, 4.31 and 4.31 on using reagents II, III and IV, respectively and the optimum pHs for Meb are 4.21,4.31 and 7.29 with reagents II, III and IV respectively.

(ii) An evidence for complex formation between drug and reagent molecules is observed in the maximum wavelength (λ_{max})of coloured complexes formed under the optimum conditions. It possesses a red shift from that of the pure reagent or drug under the same conditions.

Sul complexes with reagents I, III and IV absorb maximally at 550, 440 and 450 nm, respectively. Lin complexes have λ_{max} at 525, 428 and 440 nm for reagents II, III and IV, respectively. For Meb complexes with reagents II,

III and IV, the maximum wavelengths are 525, 428 and 450 nm, respectively.

(iii) Study of the effect of time and temperature showed that complexes are formed simultaneously and remain stable for about 2 hs. Also, the obtained complexes are stable to heating up to 45 ^{0}C.

(iv) The sequence of addition was found to be of significant importance where it was found that the best sequence of addition is Drug-Buffer-Reagent in the majority of cases. Thus, it can be concluded that buffered media are required to obtain the drug molecule in the suitable form for complex formation.

(v) The stoichiometry of the complexes formed in solution was detected using the mole ratio and continuous variation methods. It was found that all complexes are of 1:1 stoichiometric ratio except that of Lin with reagent II where both 1:1 and 2:1 (D/R) ratios were formed.

The stability constants of the drug-reagent complexes were calculated from spectral data of the mole ratio and continuous variation methods. It was found that the stability of the formed complexes runs in the order Lin-II > Sul-I > Lin-III > Sul-III > Sul-IV > Meb-II > Meb-III > Lin-IV > Meb-IV.

(vi) The optimum concentrations of drugs which can be successfully determined using the reagents under study, were detected by ***Beer***'s law. From the data obtained, it was found that Sul was successfully determined up to 50, 90 and 50 μg/mL on using reagents I, III and IV, respectively, while

Lin was determined up to 70, 70 and 50 μg/mL. Meb was determined up to 70, 60 and 30 μg/mL using reagents II, III and IV, respectively.

The values of the molar absorbtivity lies within the range 1.67 $x10^3$ - 4.10 $x10^3$, 1.24 $x10^3$ - 3.13 $x10^3$ and 4.19 $x10^3$ - 9.97 $x10^3$ L $mol^{-1}cm^{-1}$ for Sul, Lin and Meb, respectively. The high values of the molar absorbtivity obtained reflect the sensitivity of the proposed method.

(vii) Another way for detecting the lower and higher limits of concentration could be determined is the ***Ringbom*** method, where it was found that Sul can be determined with in the range 10-80 μg/mL, Lin and Meb can be determined in the range 10-60 μg/mL. A satisfactory agreement between ***Beer***'s law and ***Ringbom*** method was observed.

(viii) The presence of additives and excipients such as sodium acetate, bicarbonate, magnesium stearate, talc powder, starch, glucose, fructose and lactose was studied where it was found that they don't interfere up to 10 %.

(ix) As an application of the proposed methods, local samples of the drugs under investigation were used including:

1- Sutrim tablets and suspension manufactured by Memphis Co. for Pharmaceutical and Chemical Industries.
2- Septazole tablets and suspension manufactured by Alexandria company for Pharmaceuticals.
3- Lincocin injection sterile solution manufactured by Memphis Company.
4- Colospasmin tablets manufactured by EIPICO.

Evaluation of the accuracy and precision of the proposed methods in comparison to the official ones was in satisfactory agreement. Since the recovery was 98.7-100 % for Sul, 99.3 % for Lin and 99.5 % for Meb. R.S.D.% did not exceed 0.389 % for all drugs. The F-test and t-test values were in the acceptable range.

(x) Further support for the stoichiometries of complexes was performed by conductometric titrations. The variations of the equivalent conductance, with mL of reagent added, supported the formation of CT complex. The stoichiometric ratios sustained with results of spectrophotometric technique.

3.B. Studies of solid complexes:

In this part of study, the solid CT complexes were isolated and analyzed.

(i) The molecular composition was first determined by elemental analysis and the proposed tentative formula were determined.

(ii) The CT complexes possess two types of electronic transitions n-π^*, and π-π^*. The energy interaction of CT complexes (E_{CT}) were determined from spectral data and then used to determined the ionization potential (I_P) of each drug. The mean value for I_P of Sul is 8.46 eV and 8.56 eV for Meb.

(iii) ***Bensi-Hildebrand*** equation was applied to spectrophotometric data in order to determine the stability constants (K) and molar absoptivities (ε) of the CT complexes.

(iv) The IR spectra of CT complexes were studied and compared with those of free donors and acceptors. The stretching vibrations of NH_2, OH, C-O, S=O, and C=O groups suffer dramatic changes in positions and intensity. The explanation in previous studies are used for proving the formation of complexes and understanding the nature of bonding between the donors and acceptors.

From the data obtained, the CT interaction in such complexes are suggested to be as follow: